REMARKS

Claim 1has been amended to remove the phrase "at least" and otherwise reorder the claim for improved clarity. Claim 3 has been amended to replace the term "substantially identical" with "at least 95% identical." Claims directed to SEQ ID NOS. including a single substitution have been cancelled as inconsistent with the independent claim from which they depend. Support for increased affinity to FcRn and increased half-life is provided at p. 6, lines 13-26. Support for at least 95% sequence identity is provided at e.g., p. 18, line 9. No amendment should be construed as acquiescence in any ground of rejection. Applicants respond to the Examiner's comments using the paragraph numbering of the office action.

5. Claims 1-8, 13, and 38-41 stand rejected under 35 USC 112, second paragraph on the basis that dependent claims encompass SEQ ID NOS. having a single mutation. This matter has been corrected.

6-7. Claims 1-8, 13 and 38-41 stand rejected under 35 USC 112, first paragraph on the basis that claims 1, 2, 13, 38 and 39 refer to "at least amino acid residue 250 and amino acid residue 428" and claims 3, 4, 6-8, 40 and 41 use the term "substantially identical." The Examiner alleges that undue experimentation would be required in using the claimed mutations at position 250 and 428 in combination with other mutations to increase FcRn binding and/or serum half-life.

As a preliminary matter claim 5 does not contain either of the terms noted by the Examiner, so the rejection does not appear addressed to this claim. Applicants do not agree with the Examiner's comments but have nevertheless deleted the term "at least" from claim 1. This amendment should not, however, be construed as implying that an unmodified antibody necessarily contains naturally occurring constant regions except at positions 250 and 428. As disclosed in the specification, unmodified antibodies can include antibodies that are genetically-altered for example to provide improved stability and/or therapeutic efficacy (p. 23, lines 6-9), such as for example the IgG2M3 mutant disclosed at p. 24, line 12.

Claim 3 has been amended to specify that the claimed heavy chain constant region has at least 95% sequence identity to a naturally occurring constant region. It is respectfully submitted that such antibodies do not require undue experimentation based particularly on the state of the art and the guidance provided by the specification. As reviewed in the specification, the art provides several examples of substitutions at positions other than 250 and 428 that are known to increase FcRn binding and half-life (see specification at pp. 3-5). The art also provides other examples of substitutions at other positions known to decrease FcRn binding and/or decrease half-life (id.). As the Examiner has noted the specification provides another example, position 314, that decreases FcRn binding and half-life. The art and specification also disclose other mutations in the heavy chain constant region that are useful for reasons independent of the FcRn receptor. For example, the IgG2M3 mutation disclosed above is useful for reducing binding to FcγR receptors, thereby decreasing mitotic effects on T-cells (see US 5,834,597). Given the extensive knowledge in the art of which other substitutions besides those claimed at positions 250 and 428 cause increased binding to FcRn, and which cause decreased binding, the skilled person would have no difficulty selecting examples of substitutions from the former category and avoiding from the latter category for use with the claimed substitutions at 250 and 428 to result in an antibody having increased binding affinity for FcRn and/or increased half-life. Equally, the skilled person would have no difficulty using the claimed substitutions at positions 250 and 428 in combination with other art-known substitutions of immunoglobulin constant regions (such as Ig2M3) that are useful for reasons unrelated to FcRn binding. For these reasons, it is respectfully submitted that undue experimentation would not be required to use the claimed mutations at positions 250 and 428 together with other mutations in constant regions having at least 95% sequence identity to a naturally occurring constant region.

The Examiner also alleges that claims 1-8, 13 and 38-41 lack enablement in that daclizumab is not publicly available. In reply, it is noted that the amended claims refer only to the variable region of daclizumab and that this region is explicitly defined by SEQ ID NOS. The variable region of daclizumab can thus be reproduced from these SEQ ID NOS. without

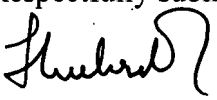
reference to a deposit or sequences contained in US 5,530,101. Nevertheless, applicants note that the antibody now known as daclizumab is referred to in the '101 patent as humanized "anti-tac" and has heavy and light chain variable region sequences shown in Figs. 15 and 16 respectively.

8-9. Applicant attaches a terminal disclaimer with respect to USSN 10/687,118 (now US 7,217,797), USSN 11/102,621 and USSN 10/966,673 (now US 7,217,798).

10-11. The present application and 10/966,673 are both commonly assigned to PDL BioPharma, Inc. The chain of title in each case has been recorded at the PTO and can be viewed on PAIR. Should the Examiner require copies of any documents in the chain of title, she is invited to contact the undersigned.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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Attachments
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